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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,554	04/03/2006	Leonardo De Maria	10508.204-US	9304

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents-US-NY@novozymes.com

Office Action Summary	Application No.	Applicant(s)	
	10/574,554	DE MARIA ET AL.	
	Examiner	Art Unit	
	WILLIAM W. MOORE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,9,11,13,15,16,21-26,28-31 and 37* is/are pending in the application.

4a) Of the above claim(s) *13 and 21-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7,9,11,15,16,28-31 and 37* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :20060403, 20081024, 20071128, 200080222, 20090408.

DETAILED ACTION

Priority

Applicant's claim in the Declaration of Inventorship and in the Application Data Sheet filed 3 April 2006 to priority under 35 U.S.C. §§ 119 and 371 of the 10 October 2003 and 1 March 2004 filing dates of the Danish patent applications, respectively, Nos. 2003-01494 and 2004-00333, as well as the US Provisional applications Nos. 60/510,450 and 60/549,347 filed, respectively 10 October 2003 and 2 March 2004, and the common successor International patent application PCT/DK2004/000688 filed 8 October 2004, of which the instant application is a continuation under 35 U.S.C. § 371, is hereby acknowledged.

Information Disclosure Statement

Applicant's Information Disclosure Statements [IDS] filed with the application on 3 April 2006, and subsequently on 24 October 2007, 28 November 2007, 22 February 2008, and 8 April 2009 are hereby acknowledged. Executed copies of the PTO-Forms 1449 submitted with each of the five IDS accompany this communication. Three journal articles were not submitted in their entirety – only a first page was provided for each – and these are lined-through on the Forms 1449 as not considered. Duplicative citations of foreign patent publications and a journal article are also lined-through on the Forms 1449.

Preliminary Amendment

Applicant's Preliminary Amendment filed 3 April 2006 has been entered, providing a cross-reference to related applications at page 1 of the specification, a revised Sequence Listing, and cancelling claims 3, 6, 8, 10, 12, 14, 17-20, 27, and 32-36. Claims 1, 2, 4, 5, 7, 9, 11, 13, 15, 16, 21-26, 28-31, and 37 remain in the application.

Election/Restrictions

Applicant's provisional election in the reply filed 31 August 2009 of the invention of Group 10 wherein claims 1, 2, 4, 7, 9, 11, 15, 16, 28-31, and 37 are each drawn in part to a variant of a parent protease that comprises at least one amino acid substitution in a region corresponding to the fourteen amino acid sequence region from position 118 through position 131 of the mature protease amino acid sequence of SEQ ID NO:2 from position 1-188, to compositions comprising same, and to methods of use thereof, is acknowledged. Applicant presents no traversal of the requirement for restriction mailed 29 July 2009 and proposes instead that five separate, widely-separated positions for substitution might be selected for examination. Since two of Applicant's proposed SEQ ID NO:2 correspondent positions, 122 and 127, are within the array of fourteen

amino acids comprising substitution sites of the elected Group 10, the adjacent amino acid sequence regions of Groups 7-9 which comprise one of Applicant's further proposed SEQ ID NO:2 correspondent positions, position 92, are also examined herein together with Group 10. Where a prior art publication discloses a substitution at any of these three positions relative to the amino acid residing at these positions in the amino acid sequence of SEQ ID NO:2, the substituting amino acid at the positions is underlined in the rejections below. Because the prior art applied in rejections below also discloses polynucleotides encoding protease variants, vectors and host cells comprising variant-encoding polynucleotides, and methods of making encoded variants using such vectors and host cells, the restriction requirement between Groups 10 and 7-9 as well as between Groups 7-10 and 24-27 is RESCINDED. The requirement for restriction as between Groups 7-10 and 24-27 on the one hand, and the remaining Groups 1-6, 11-23, and 28-51 on the other, is still deemed proper and is therefore made FINAL. No paired cysteine sets of claim 5 link positions entirely within the SEQ ID NO:2 correspondent positions of Groups 7-10 but claim 5 is examined herein insofar as one member of a cysteine pair is required within positions Groups 7-10. No position indicated in claim 13 is found in any of Groups 7-10, thus claims 1, 2, 4, 5, 7, 9, 11, 15, 16, 21-25, 28-31 and 37 are examined herein to the extent that they describe proteases sharing at least 60% amino acid sequence identity with SEQ ID NO:2 and differing from the amino acid sequence of SEQ ID NO:2, which can be considered a "parent protease", at one or more of 44 amino acid positions within the arrays that correspond to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2.

Objection to the Specification

The disclosure is objected to because it contains embedded hyperlinks, or another form of browser-executable code, at pages 4, 5, and 12 at, respectively, lines 36, 12, and 8. Applicant is required to delete the embedded hyperlinks or other forms of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims are objected to because of the following informalities: Claims 7, 9, and 11 are objected to because they fail to recite their positions for amino acid substitutions in numerical order, preventing the public from readily distinguishing the intended substitutions. See claims 2, 4, 15, and 16, not subject to this objection. Appropriate correction is required, e.g., amending

claim 7 to recite "7P; 13P; 23P; 24P; 25P; 27P; 81P; 82P; 92P; 93P; 94P; 96P; 98P; 105P; 125P; 135P; 136P; 151P; 174P; 175P; 176P; 184P; and/or 187P";

claim 9 to recite "10E,D; 12E,D; 13E,D; 42E,D; 46E,D; 47E,D; 58E,D; 69E,D; 70E,D; 81E,D; 82E,D; 84E,D; 89E,D; 95E,D; 96E,D; 113E,D; 120E,D; 129E,D; 130E,D; 140E,D; 150E,D; 151E,D; 160E,D; 161E,D; and/or 166E,D"; and

claim 11 to recite "24R,K; 25R,K; 39R,K; 56R,K; 72R,K; 92R,K; 97R,K; 99R,K; 111R,K; 118R,K; 122R,K; 124R,K; 127R,K; 162R,K; 180R,K; 181R,K; and/or 188R,K".

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 30 is rejected under 35 U.S.C. § 101 because the disclosed invention is inoperative and therefore lacks utility. Claim 30 is drawn to a "method for improving the nutritional value of an animal feed" but fails to describe any method, i.e., there are no method steps in the claim that might tend to provide the result desired in the claim preamble. Merely reciting "wherein the protease variant of claim 1" cannot define an operative method where any method requires at least one process step.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 16, and 30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15 and 16 are indefinite where the term "preferably", which occurs in the closing phrase of each of claims 15 and 16, and also appears in several parenthetical statements within claim 16, because it is unclear whether limitation(s) in phrases beginning with "preferably" are the same invention of the claims. See MPEP § 2173.05(d). In this national forum, the proper form for presenting multiple, related, subject matters in patent claims is to provide **separate** claims of different scope where (an) initial claim(s) describe(s) only the subject matter having the broadest scope now present in each of the rejected claims and is followed by one or more dependent claim(s) each referring back to the initial claim and describing subject matter(s) of progressively lesser scope, such as those that now follow the term "preferably" in claims 15 and 16, and wherein no claim recites the term "preferably" or a similar term.

Claim 30 is rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: A method step that could provide the result that is required by the claim preamble. The claim fails to recite any method step, such as a step of adding the protease to the animal feed. See, e.g., claim 31, not subject to this rejection.

Claim 30 is separately rejected under 35 U.S.C. § 112, second paragraph, as indefinite because there is no antecedent basis for the recitation "wherein the protease of claim 1". The artisan and they public seeking to determine the relationship of a protease to the method indicated in the claim preamble cannot establish its role. However, for the purpose of applying prior art in the following rejections, the claim is construed as though it had cited at least one method step following the recitation of "feed", viz., "comprising the step of adding the protease variant of claim 1 to the animal feed".

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 USC § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The following is a quotation of 35 USC § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 identifies no particular "parent protease", and only claim 16 identifies any amino acids that might be present in the amino acid sequence of a "parent protease", thus the prior art applied in the following rejections is applied as though SEQ ID NO:2 herein were the particular "parent protease" with which amino acid sequence variation is determined.

A. Claims 1, 2, 4, 16, and 21 are rejected under 35 U.S.C. § 102(b) as being anticipated by Moriyama et al., **JP 2003-284571**, made of record with Applicant's IDS.

Published 7 October 2003, Moriyama et al. disclose in their SEQ ID NO:2 the mature, 188 amino acid, sequence of a *Nocardiopsis sp*. TOA-1 protease useful for degrading proteins and sharing 89% identity with SEQ ID NO:2 herein, differing therefrom by twelve relative amino acid substitutions: **T82S**, **A89S**, **H91S**, **N92S**, **Q93T**, **S99Q**, **G118N**, **S120T**, **E125Q**, **T129H**, **N130S** and **M131L**. Moriyama et al. also disclose that their TOA-1 protease acts on insoluble protein, including the animal protein keratin, thus is suitable for incorporation in detergent compositions and useful in food processing. See paragraphs 0002, 0004-0007, 0009 and clause (a) of claim 1 of the English-language translation provided with Applicant's IDS. Because the instant application indicates at page 8, lines 23-24, that a "variant" protease is a protease that is not identical to SEQ ID NO:2 herein, the protease of SEQ ID NO:2 of Moriyama et al. meets the limitations of claims 1, 2, 4, and 16 herein. Moriyama et al. also disclose a nucleic acid sequence, SEQ ID NO:1, that encodes the integral precursor protease comprising the mature protease amino acid sequence within their SEQ ID NO:2, meeting limitations of claim 21 herein.

B. Claims 1, 2, 4, 16, and 28-31 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sjøholm et al., **WO 01/58276**, and **US 6,855,548**, both made of record with Applicant's IDS.

Sjøholm et al., **WO 01/58276**, and Sjøholm et al., **US 6,855,548** are identical disclosures. Sjøholm et al. **'548** was published 15 February 2005, more than a year before the 3 April 2006 filing date of the instant application. Both of Sjøholm et al. **'276** and **'548** disclose the mature, 188 amino acid, sequence of a *Nocardiopsis sp*. NRRL 18262 protease in their SEQ ID NO:1 that is 99.5% identical to SEQ ID NO:2 herein, differing by the relative amino acid substitution **T82A**. Because the instant application indicates at page 8, lines 23-24, that a "variant" protease is protease that is not identical to SEQ ID NO:2 herein, the protease of SEQ ID NO:1 of Sjøholm et al. meets limitations of claims 1, 2, 4, and 16 herein. Sjøholm et al. also disclose preparation of animal feed additives comprising the protease of their SEQ ID NO:1 and at least one each of a fat-soluble vitamin, a water soluble vitamin, and a trace mineral, or all three, that may be formulated in animal feed compositions having a crude protein content of 50 to 800 g/kg which, when added to such compositions, improve their nutritional value, and further disclose a method for the treatment of proteins comprising the addition of the protease of their SEQ ID NO:1, meeting limitations of claims 28-31 herein. See col. 5, line 49, through col. 11, line 55; col. 13, lines 9-26; col. 16, line 49, through col. 22, line 61; and claims 1-6 of the **'548** patent.

C. Claims 1, 2, 4, 11, 15, 16, 21-25, 28-31, and 37 are rejected under 35 U.S.C. § 102(e) as being anticipated by Lassen et al., **US 7,179,630**, made of record with Applicant's IDS.

The 188-amino acid sequences of the *Nocardiopsis alba* 15647 protease of SEQ ID NO:12 and the *Nocardiopsis dassonvillei* DSM 43235 protease of SEQ ID NO:2 of Lassen et al. **'630**

have priority of the 20 June 2003 filing date of both, respectively, the US provisional applications 60/480,024 and 60/480,096, thus these protease sequences and other disclosures of these two provisional applications represented within the **'630** patent disclosure are available as prior art under 35 U.S.C. § 102(e), particularly where page 9 of the '096 priority document, and page 10 of the '024 priority document, disclose that a "variant" differs from either SEQ ID NO:2 or SEQ ID NO:12 of the patent, "by an insertion or deletion of one or more amino acid residues" and where the instant specification indicates at page 8, lines 23-24, that a "variant" protease is protease that is not identical to SEQ ID NO:2 herein. The mature protease of SEQ ID NO:12 of Lassen et al. **'630** is 87.4% identical to SEQ ID NO:2 herein and differs from SEQ ID NO:2 herein by the relative amino acid substitutions **A89S**, **H91S**, **N92S**, **P95A**, **S99Q**, **V100**I, I**114V**, **S120T**, **E125Q**, **T129Q**, and **M131L**, while the mature protease of SEQ ID NO:2 of Lassen et al. **'630** is 85.8% identical to SEQ ID NO:2 herein and differs from SEQ ID NO:2 herein in the relative amino acid substitutions **T82S**, **A86Q**, **T87S**, **A89T**, **H91T**, **N92S**, I**96A**, **S99A**, **G118N**, **S120T**, **S122R**, **E125Q**, **T129Y**, **N130S** and **M131L** where each of the bold font relative substitution meet limitations of claims 1, 2, 4, and 16 herein, and the underlined relative S122R substitution also meets limitations of claims 11 and 15 herein. In addition, Lassen et al. **'630** disclose that their proteases may include both "conservative amino acid substitutions that do not significantly affect the folding and/or activity of the protein[and] small deletions, typically of one to about 30 amino acids", where "conservative substitutions [may be] within the group[s] of basic amino acids (arginine, lysine and histidine), acidic amino acids (glutamic acid and aspartic acid), polar amino acids (glutamine and asparagine), hydrophobic amino acids (leucine, isoleucine and valine), aromatic amino acids (phenylalanine, tryptophan and tyrosine), and small amino acids (glycine, alanine, serine, threonine and methionine) [where t]he most commonly occurring exchanges are Ala/Ser, Val/**I**le, Asp/Glu, Thr/Ser, Ala/Gly, Ala/Thr, Ser/Asn, Ala/Val, Ser/Gly, Tyr/Phe, Ala/Pro, Lys/Arg, Asp/Asn, Leu/**I**le, Leu/Val, Ala/Glu, and Asp/Gly as well as these in reverse". See page 10, lines 5-14 of the '096 priority application and col. 2, line 18, through col. 3, line 24, and col. 19, line 41, through col. 20, line 24, of the **'630** patent.

Lassen et al. **'630** also disclose the preparation of nucleic acid constructs comprising polynucleotides encoding each protease amino acid sequence operably linked to one of more nucleic acid control sequences capable of directing the production of each encoded protease in suitable expression hosts, recombinant expression vectors comprising such nucleic acid constructs, recombinant host cells comprising such nucleic acid constructs, and methods for recombinant production of either protease by cultivating the host cells to produce supernatants comprising either protease and recovering the proteases, meeting limitations of claims 21-25

herein. See page 15, line 28, through page 25, line 16, of the '096 priority document. Lassen et al. **'630** further disclose preparation of animal feed additives comprising either of the proteases of their SEQ ID NO:2 or their SEQ ID NO:12 and at least one of each of a fat-soluble vitamin, a water soluble vitamin, and a trace mineral, which are formulated in animal feed compositions having a crude protein content of 50 to 800 g/kg, which additives improve the nutritional value of an animal feed composition when added to such a composition, and disclose as well a method for the treatment of proteins comprising addition of either of the proteases of their SEQ IDs NOs:2 and 12, meeting limitations of claims 28-31 herein. See page 5, line 32, through page 35, line 55, of their '096 priority document. Lassen et al. **'630** additionally disclose preparation of detergent compositions that comprise either of the proteases of their SEQ IDs NOs:2 and 12 at page 35, line 22, through page 38, line 27, meeting limitations of claim 37 herein.

D. Claims 1, 2, 4, 11, 15, 16, 21-25, 28-31, and 37 are rejected under 35 U.S.C. § 102(e) as being anticipated by Lassen, **US 7,485,447**, made of record herewith.

The amino acid sequences of the mature *Nocardiopsis prasina* DSM 15649 protease of SEQ ID NO:41, the mature *Nocardiopsis prasina* DSM 15648 protease of SEQ ID NO:37, the mature *Nocardiopsis alba* DSM 15647 protease of SEQ ID NO:33, and the mature *Nocardiopsis dassonvillei* DSM 43235 protease of SEQ ID NO:28 of Lassen **'447** have the priority of the 20 June 2003-filed US provisional application 60/480,103. Thus these amino acid sequences, that are identically numbered in the provisional application and the **'447** patent, as well as the other disclosures of the provisional application represented within the **'447** patent disclosure are all available as prior art under 35 U.S.C. § 102(e), particularly where page 3, lines 21-24, of the '103 priority document discloses that a "variant" differs from any of SEQ IDs NOs:28, 33, 37, or 41 "by an insertion or deletion of one or more amino acid residues" and where the instant specification indicates at page 8, lines 23-24, that a "variant" protease is protease that is not identical to its SEQ ID NO:2. Lassen **'447** also discloses that such amino acid substitutions include both "conservative amino acid substitutions that do not significantly affect the folding and/or activity of the protein[and] small deletions, typically of one to about 30 amino acids", where "conservative substitutions [may be] within the group[s] of basic amino acids (arginine, lysine and histidine), acidic amino acids (glutamic acid and aspartic acid), polar amino acids (glutamine and asparagine), hydrophobic amino acids (leucine, isoleucine and valine), aromatic amino acids (phenylalanine, tryptophan and tyrosine), and small amino acids (glycine, alanine, serine, threonine and methionine) [where t]he most commonly occurring exchanges are Ala/Ser, Val/Ile, Asp/Glu, Thr/Ser, Ala/Gly, Ala/Thr, Ser/Asn, Ala/Val, Ser/Gly, Tyr/Phe, Ala/Pro, Lys/Arg, Asp/Asn, Leu/Ile, Leu/Val, Ala/Glu, and Asp/Gly as well as these in reverse". See page 11 of

the '103 priority document and col. 8, line 65, through col. 9, line 25 of the **'447** patent. The mature proteases of SEQ IDs NOs:37 and 41 of Lassen **'447** are, respectively, 98.6% and 99.4% identical to the amino acid sequence of SEQ ID NO:2 but are identical thereto within the sets of contiguous amino acid sequence positions corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131**. The mature protease of SEQ ID NO:33 of Lassen **'447** is 87.4% identical to SEQ ID NO:2 herein and differs therefrom by the relative amino acid substitutions **A89S**, **H91S**, **N92S**, **P95A**, **S99Q**, **V100**I, I**114V**, **S120T**, **E125Q**, **T129Q**, and **M131L**, while the mature protease of SEQ ID NO:28 of Lassen **'447** is 87.4% identical to SEQ ID NO:2 herein and differs therefrom by the relative amino acid substitutions **T82S**, **A86Q**, **T87S**, **A89T**, **H91T**, **N92S**, I**96A**, **S99A**, **G118N**, **S120T**, **S122R**, **E125Q**, **T129Y**, **N130S** and **M131L** where each of the bold font relative substitution meet limitations of claims 1, 2, 4, and 16 herein, and the underlined relative S122R substitution also meets limitations of claims 11 and 15 herein. Lassen **'447** further discloses (i) the preparation of nucleic acid constructs comprising polynucleotides encoding each of the protease amino acid sequences operably linked to one of more nucleic acid control sequences capable of directing the production of each encoded protease in suitable expression hosts, recombinant expression vectors comprising such nucleic acid constructs, recombinant host cells comprising such nucleic acid constructs, and methods for recombinant production of each protease by cultivating the host cells to produce supernatants comprising either protease and recovering the proteases, as well as (ii) animal feed additives and compositions comprising each protease and at least one fat soluble vitamin, at least one water soluble vitamin, at least one trace mineral, and a crude protein contend of 50 to 800 g/kg, and a method for improving the nutritional value of such animal feed compositions by incorporating each protease therein, as well as (ii) a method for treating proteins by adding such variants, and (iv) preparing a detergent formulation including the proteases and a surfactant according to claims 21-25, 28-31, and 37 herein. See page 4, lines 7-32, and pages 40-41 of the '103 priority document and at col. 13, line 16, through col. 20, line 57, and at col. 23, line 55, through col. 29, line 35, col. 29, line 40, through col. 32, line 12.

The applied references Lassen **US 7,485,447**, and Lassen et al., **US 7,179,630**, have at least one common inventor with the instant application. Based upon the earlier effective U.S. filing dates of these references based on several of their priority provisional applications, they constitute prior art under 35 USC § 102(e). This rejection under 35 USC § 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

E. Claims 1, 2, 4, 9, 15, 16, 21-25, 28-31, and 37 are rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Lassen, **US 7,485,447**, discussed above.

This rejection is directed to variant proteases of claims 1, 2, 4, 11, 15, and 16 that differ from SEQ ID NO:2 of the instant application in view of the disclosure of Lassen **'447** that certain preferred, conservative, amino acid substitutions are suitable for amino acids that are present in the amino acid sequence positions that correspond to the amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** in mature proteases of SEQ IDs NOs:37 and 41 of Lassen **'447** and that are the same amino acids found at the corresponding positions in the amino acid sequence of SEQ ID NO:2 herein. The disclosure at page 11 of the '103 priority document and at col. 8, line 65, through col. 9, line 25 of the **'447** patent, discussed above, is taken as before, i.e., that any amino acid within the region elected by Applicant, together the further regions examined herein, may be replaced by "conservative amino acid substitutions that do not significantly affect the folding and/or activity of the protein[and] small deletions, typically of one to about 30 amino acids", where "conservative substitutions [may be] within the group[s] of basic amino acids (arginine, lysine and histidine), acidic amino acids (glutamic acid and aspartic acid), polar amino acids (glutamine and asparagine), hydrophobic amino acids (leucine, isoleucine and valine), aromatic amino acids (phenylalanine, tryptophan and tyrosine), and small amino acids (glycine, alanine, serine, threonine and methionine) [where t]he most commonly occurring exchanges are Ala/Ser, Val/Ile, Asp/Glu, Thr/Ser, Ala/Gly, Ala/Thr, Ser/Asn, Ala/Val, Ser/Gly, Tyr/Phe, Ala/Pro, Lys/Arg, Asp/Asn, Leu/Ile, Leu/Val, Ala/Glu, and Asp/Gly as well as these in reverse". Thus Lassen et al. are considered to inherently disclose the following amino acid substitutions in the amino acid sequence of SEQ ID NO:2 indicated by claims 1, 2, 4, 7, 9, 15, and 16 herein:

S78A, S78T, S78G, S78N;
R79K;
Y80F;
N81S, N81D (includes claim 9);
T82A, T82S;
G83A, G83D, G83S;
G84A, G84D, G84S (includes claims 9 and 15);
Y85F;
A86S, A86G, A86T, A86V, A86P, A86E;
T87S, T87A;
V88 **I**, V88A, V88L;
A89S, A89G, A89T, A89V, A89P, A89E (includes claim 9);
G90A, G90D, G90S;
H91K, H91R (claims 1 and 2 only);

N92S, N92D (claims 1 and 2 only);
Q93N (claims 1 and 2 only);
A94P (includes claim 7);
P95A (claims 1 and 2 only);
I 96L (claims 1 and 2 only);
G97A, G97D, G97S (claims 1 and 2 only);
S98N, S98T, S98G, S98A (claims 1 and 2 only);
S99A;
V100 **I** (claims 1 and 2 only);
R103K (claims 1 and 2 only);
G104A, G104D, G104S (claims 1 and 2 only);
S105T, S105N, S105G, S105A (claims 1 and 2 only);
T106A, T106S (claims 1 and 2 only);
G112A, G112D, G112S (claims 1 and 2 only);
T113S, T113A (claims 1 and 2 only);
I 114L, **I** 114V (claims 1 and 2 only);
G118N (see claim 16);
Q119N (claims 1 and 2 only);
S120A, S120T, S120G, S120N (claims 1 and 2 only);
V121 **I** (claims 1 and 2 only);
S122A, S122T, S122G, S122N (claims 1 and 2 only);
Y123F (claims 1 and 2 only);
P124A (claims 1 and 2 only);
E125D (claims 1 and 2 only);
G126A, G126D, G126S (claims 1 and 2 only);
T127S, T127A (claims 1 and 2 only);
V128 **I** (claims 1 and 2 only);
T129A, T129A (claims 1 and 2 only);
N130S, N130D (includes claim 9); and
M131L (see claim 16).

In the alternative, insofar as Lassen **'447** did not prepare variants of their SEQ IDs NOs:37 and 41 that comprise one of more of their preferred, disclosed, substitutions, it would have been obvious to one of ordinary skill in the art to make one of more of these substitutions, whether in the amino acid sequences of SEQ IDs NOs:37 and 41 of Lassen **'447**, or in the amino acid sequence of SEQ ID NO:2 herein, where (1) all three are identical within the region comprising the amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2 herein and (2) the amino acid sequence of SEQ IDs NOs:28 and 33 of Lassen **'447** clearly show that many of the preferred substitutions taught by Lassen **'447** are appropriate for, and may be introduced

at more than one of, the amino acid positions within this region, providing one of ordinary skill in the art with a reasonable expectation of success in practicing the claimed invention.

Claims 21-25, 28-31, and 37 are included in this rejection because the disclosure/teaching of Lassen **'447** with respect to preferred substitutions is considered equally to extend to (i) the preparation of nucleic acid constructs comprising polynucleotides encoding any of such variant protease amino acid sequences operably linked to one of more nucleic acid control sequences capable of directing the production of each encoded protease in suitable expression hosts, recombinant expression vectors comprising such nucleic acid constructs, recombinant host cells comprising such nucleic acid constructs, and methods for recombinant production of such variant proteases by cultivating the host cells to produce supernatants comprising any of the variant proteases and recovering the variant proteases, as well as (ii) animal feed additives and compositions comprising each variant proteases and at least one fat soluble vitamin, at least one water soluble vitamin, at least one trace mineral, and a crude protein contend of 50 to 800 g/kg, and a method for improving the nutritional value of such animal feed compositions by incorporating such variant proteases therein, as well as (ii) a method for treating proteins by adding such variants proteases, and (iv) preparing detergent formulations including such variant proteases and a surfactant, according to claims 21-25, 28-31, and 37 herein.

The applied reference, Lassen, **US 7,485,447**, has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 USC § 102(e). This rejection under 35 USC § 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 USC § 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 USC § 103(c) as prior art in a rejection under 35 USC § 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

F. Claims 22-25, 28-31, and 37 are rejected under 35 USC § 103(a) as being unpatentable over Moriyama et al., **JP 2003-284571**, as applied to claims 1, 2, 4, 16, and 21 above, in view of Wilson et al., **US 5,705,379**, and Anderson et al., **EP 0 506 448**, both made of record with Applicant's IDS, and Sjøholm et al., **WO 01/58276**, discussed above.

The teachings of Moriyama et al., discussed above, are taken as before. Wilson et al. teach the preparation of a nucleic acid sequence encoding a precursor protease that comprises

a 194-amino acid mature protease having an amino acid sequence that is 47% identical to SEQ ID NO:2 herein, as well as the preparation of nucleic acid constructs that comprise the protease-encoding nucleic acid sequence operably linked to nucleic acid sequence regions that control the transcription and translation of the protease-encoding nucleic acid sequence and directing its expression in a host cell, expression vectors comprising such recombinant DNA molecules, recombinant host cells comprising such expression vectors, and methods for the recombinant production of the encoded protease and its recovery from the cells. See col. 2, line 36, through col. 4, line 6, and col. 5, line 1, through col. 12, line 64, as well as claims 2-8. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a nucleic acid sequence encoding the TOA-1 protease of Moriyama et al. in a nucleic acid construct, expression vector, and host cell of Wilson et al., and to practice a method of making the TOA-1 protease recombinantly utilizing such a host cell and recovering the recombinantly-produced host cell according to claims 22-25 herein. This is because Wilson et al. teach nucleic acid constructs, expression vectors, and host cells often-used in the art to recombinantly produce proteases having commercial utility, such as the TOA-1 protease that Moriyama et al. teach has commercial utility and because, based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success in practicing the claimed invention.

The teachings of Moriyama et al. in paragraphs 0002, 0004-0007, 0009 and clause (a) of claim 1 of the English-language translation, discussed above, that their TOA-1 protease acts on insoluble protein, including the animal protein keratin, thus is suitable for incorporation in detergent compositions and useful in food processing, are taken as before. Similarly the teachings Sjøholm et al., **WO 01/58276**, of the preparation of animal feed additives comprising the protease of their SEQ ID NO:1 and at least one each of a fat-soluble vitamin, a water soluble vitamin, and a trace mineral that may be formulated in animal feed compositions having a crude protein content of 50 to 800 g/kg which, when added to such compositions, improve their nutritional value, and further teaching of a method for the treatment of proteins comprising the addition of the protease discussed above, are now taken as before. It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the TOA-1 protease of Moriyama et al. in the feed additives of Sjøholm et al., to formulate such additives comprising the TOA-1 protease of Moriyama et al., and to add such additives to animal feed compositions having a crude protein content of 50 to 800 g/kg to improve their nutritional value, and obvious as well to such an artisan to use the TOA-1 protease of Moriyama et al. in a

method for treating proteins, meeting the limitations of claims 28-31 herein, because Moriyama et al. teach that their TOA-1 protease is particularly suitable for degrading keratin, an insoluble animal protein. The teaching of Moriyama et al. that the TOA-1 protease is a member of a class of proteases useful in detergent compositions is now emphasized. Anderson et al. teach that detergent compositions comprising proteases are formulated with surfactants. See pages 5 and 6 and claim 1. It would also have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the TOA-1 protease in detergent compositions comprising a surfactant, meeting the limitations of claim 37 herein, because Moriyama et al. teach that a TOA-1 protease is a member of the class of proteases useful in detergent compositions and Anderson et al. teach that different proteases are advantageously incorporated in detergent compositions that comprise surfactants. Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success in practicing the claimed invention.

Claims 21-25 and 37 are rejected under 35 USC § 103(a) as being obvious over Sjøholm et al., **WO 01/58276**, as applied to claims 1, 2, 4, 16, and 28-31 above, in view of Wilson et al., **US 5,705,379**, and Anderson et al., **EP 0 506 448 A1**, both discussed above.

The teachings of Sjøholm et al., discussed above, are taken as before. Wilson et al. teach the preparation of a nucleic acid sequence encoding a precursor protease that comprises a 194-amino acid mature protease having an amino acid sequence that is 47% identical to SEQ ID NO:2 herein, as well as the preparation of nucleic acid constructs that comprise the protease-encoding nucleic acid sequence operably linked to nucleic acid sequence regions that control the transcription and translation of the protease-encoding nucleic acid sequence and directing its expression in a host cell, expression vectors comprising such recombinant DNA molecules, recombinant host cells comprising such expression vectors, and methods for the recombinant production of the encoded protease and its recovery from the cells. See col. 2, line 36, through col. 4, line 6, and col. 5, line 1, through col. 12, line 64, as well as claims 2-8. It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a nucleic acid sequence encoding the *Nocardiopsis sp*. NRRL 18262 protease of Sjøholm et al. and to incorporate the protease-encoding nucleic acid sequence in a nucleic acid construct, expression vector, and host cell of Wilson et al., and to practice a method of making the *Nocardiopsis sp*. NRRL 18262 protease recombinantly utilizing such a host cell in order to recover it from the host cell, meeting limitations of claims 21-25 herein. This is because Sjøholm et al. teach that their *Nocardiopsis sp*. NRRL 18262 protease has utility in the animal husbandry industry and Wilson et al. teach that incorporating nucleic acid sequences encoding

proteases having industrial utility in nucleic acid constructs, expression vectors, and host cells is common practice in the art in order to recombinantly produce proteases having commercial utility and because, based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success in practicing the claimed invention.

The teachings of Sjøholm et al. of their purification of the *Nocardiopsis sp*. NRRL 18262 protease, and their performance of assays that compare the pH-activity profiles, pH-stability and temperature-activity profiles of the *Nocardiopsis sp*. NRRL 18262 protease and two prior art subtilisins, the "Novo", aka subtilisin BPN', and Savinase™ proteases, at pages 22-27, Tables 1 and 2 at page 28, and Figures 1-3, are now emphasized where Figures 1-3 show one of ordinary skill in the art at the time the invention was made that the NRRL 18262 protease of Sjøholm et al. has (i) similar thermal stability with the two prior art subtilisins, (ii) an equivalent pH-activity profile over nearly the same range of alkaline pH as the two subtilisins, and (iii) a better pH-activity profile over a range of acidic pH than the two subtilisins. Anderson et al. teach that detergent compositions comprising either of the subtilisin BPN' and Savinase™ proteases together with surfactants are well known in the art, see page 2, and that other proteases having equivalent thermal stability and equivalent pH-activity profile over a broad range of alkaline pH are likewise advantageously incorporated in detergent compositions together with surfactants. See pages 5 and 6 and claim 1. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the *Nocardiopsis sp*. NRRL 18262 protease of Sjøholm et al. in a detergent composition together with a surfactant, meeting limitations of claim 37, because Sjøholm et al. teach that their protease shares performance characteristics similar to those of two prior art subtilisins often incorporated with surfactants in detergent compositions, and because Anderson et al. teach that separate microbial protease that does not share a corresponding degree of sequence similarity with the with the same two prior art subtilisins often incorporated with surfactants in detergent compositions is advantageously incorporated in detergent compositions with surfactants because it shares similar performance characteristics. Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success in practicing the claimed invention.

Double Patenting: Non-Statutory

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent

possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b)..

a. Claim 30 herein is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of Sjøholm et al., **US 6,855,548**, discussed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 30 herein is drawn to a method for improving the nutritional value of an animal feed requiring a protease variant of claim 1, which variant may differ from the protease having the amino acid sequence of SEQ ID NO:2 herein in at least one position that may be position 87 according to the pending claims 1 and 2 and the different amino acid may be alanine, according to the pending claims 4 and 16, and because the patented claim is drawn to a method for improving the nutritional value of an animal feed requiring a protease wherein a relative substitution of alanine occurs in the amino acid sequence of a protease of SEQ ID NO:1 of the patent at the position corresponding to position 87 of SEQ ID NO:2 herein but SEQ ID NO:1 of the patent is otherwise identical to the amino acid sequence of SEQ ID NO:2 herein.

b. Claims 1, 2, 4, 16, 21-25, 31, and 37 herein are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of **US 6,855,548**, discussed above, in view of the teachings of Wilson et al., **US 5,705,379**, and Anderson et al., **EP 0 506 448**, both made of record with Applicant's IDS. The teaching of claims 1-6 of the **'548** patent is taken as before. Wilson et al. teach the recombinant production of an isolated, mature, microbial serine protease having a 194-amino acid sequence that is both thermostable and active over a broad alkaline pH range by preparing a nucleic acid construct that links the region of their isolated nucleic acid sequence of their SEQ ID NO:1 that encodes a microbial serine protease precursor of their SEQ ID NO:5 to control sequences that can direct the expression of the protease-encoding DNA region in a host cell, placing the construct in an expression vector, transforming a suitable host cell with the expression vector, cultivating the host cell to permit

production of the protease whereby the mature protease is produced in the supernatant, and then recovering and isolating the protease so that it may be used in industrial processes. See col. 5 at lines 6-45, the Examples 3-5 at cols. 8-12, and claims 1-8. Wilson et al. further teach that their recombinantly-produced, isolated, mature protease "may be used as an additive to detergent solutions requiring enzyme activity in a pH range of from about 7 to about 10 to remove protein-based stains". See col. 13 at lines 5-9. Wilson et al. do not, however, teach the formulation of detergent compositions comprising a surfactant as well as their mature protease, thus Anderson et al. are now cited for teaching the preparation of detergent compositions that comprise any of several surfactants and any of several wild-type and variant mature, microbial, thermostable proteases that are also stable at alkaline pH. See page 5, line 9, through page 13, line 24. It would have been obvious to one of ordinary skill in the art to prepare a nucleic acid construct linking a DNA sequence encoding the protease of Sjøholm et al. **'548** to (a) control sequence(s) that can direct the expression of the protease-encoding DNA region in a host cell, place the construct in an expression vector, transform a suitable host cell with the expression vector, cultivate the host cell to permit production of the encoded protease whereby the mature protease is produced in the supernatant, and to then recover and isolate the protease so that it may be used in industrial processes, according to the teachings of Wilson et al., meeting limitations of claims 1, 2, 4, 16, and 21-25 herein where the protease of Sjøholm et al., **'548** isolated after a method of recombinant production of Wilson et al. constitutes a variant of SEQ ID NO:2 herein in at least one position that may be position 87 according to the pending claims 1 and 2 and the different amino acid may be alanine, according to the pending claims 4 and 16. This is because Sjøholm et al., **'548** teach at least one industrial application for their microbial protease and because Wilson et al. teach that industrially useful proteases are advantageously recombinantly produced by transformed host cells and recovered from a supernatant of the cultured host cells. It would have been further obvious to such an artisan to practice a method of treating proteins by adding the protease of Sjøholm et al. **'548** to a composition for treating proteins, which may be a detergent composition according to Wilson et al. that comprises a surfactant, meeting limitations of claim 31 and 37 herein. This is because Wilson et al. teach that thermostable, alkaline pH-stable, microbial proteases, and their variants, that are useful in industrial processes are advantageously combined with surfactants in detergent compositions.

c. Claims 1, 2, 4, 11, 15, 16, 21-25, 28-31, and 37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of **US 7,179,630**, discussed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims are drawn to a variant of a mature protease

the amino acid sequence of which shares at least 60% identity with SEQ ID NO:2 herein and may diverge from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2, a nucleic acid sequence that encodes such a variant, an expression construct comprising such a coding sequence, an expression vector that comprises such an expression construct, a recombinant host cell comprising such a vector, a method of making the encoded variant comprising cultivating such a host cell and recovering the protease variant, an animal feed additive comprising such a variant and at least one of three further components, i.e., a fat soluble vitamin, a water soluble vitamin, or a trace mineral, an animal feed composition that comprises such a feed additive as well as a crude protein content in the range of 50 to 800 g/kg, a method for improving the nutritional value of an animal feed by adding such a protease variant to the feed, a method for treating proteins comprising adding the protease variant to the proteins, and a detergent composition comprising such a protease variant, and because and because the patented claims 1-7 and 9-12 are drawn to an isolated protease, or variant thereof, having an amino acid sequence at least 95% to 99% identical to the sequence of positions 1-188 of SEQ ID NO:2 of the patent, a protease that meets the limitations of claims 1, 2, 4, 11, 15, and 16 herein where it is the same *Nocardiopsis dassonvillei* DSM 43235 protease of SEQ ID NO:2 of Lassen et al. **'630**, discussed above, while the patented claims 13-20 are drawn to an animal feed additive comprising such a protease or variant and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral according to claim 28 herein which, when added to an animal feed composition of the patented claim 15 will improve the nutritional value of such an animal feed according to claim 30 herein and will inherently constitute a method of treating proteins according to claim 31 herein where, according to the patented claims 14-16, may have a crude protein content in the range of 50 to 800 g/kg, meeting limitations of claim 29 herein, and also because the patented claim 18 requires that a detergent composition comprise a surfactant and protease of the patented claim 1 that, as noted previously, meets limitations of claims 1, 2, 4, 11, 15, and 16 herein, thus is a detergent composition of claim 37 herein.

d. Claims 21-25 herein are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over at least claim 1 of **US 7,179,630**, in view of Wilson et al., **US 5,705,379**, discussed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims 21-25 are drawn a nucleic acid sequence that encodes a protease variant having at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and

118-131 of SEQ ID NO:2, an expression construct comprising such a coding sequence and control regions, an expression vector comprising such a construct, a recombinant host cell that comprises such a vector, a method of making the encoded variant comprising cultivating such a host cell and recovering the protease variant and because at the patented claim 1 is drawn to an isolated protease, or variant thereof, having an amino acid sequence that is at least 95% identical to the sequence of positions 1-188 of SEQ ID NO:2 of the patent, a protease that meets the limitations of claims 1, 2, 4, 11, 15, and 16 herein. The teachings of Wilson et al. are taken as before. It would have been obvious to one of ordinary skill in the art to prepare a nucleic acid construct linking a DNA sequence encoding the protease of Lassen et al. **'630** to (a) control sequence(s) that can direct the expression of the protease-encoding DNA region in a host cell, place the construct in an expression vector, transform a suitable host cell with the expression vector, cultivate the host cell to permit production of the encoded protease whereby the mature protease is produced in the supernatant, and to then recover and isolate the protease so that it may be used in industrial processes, according to the teachings of Wilson et al., meeting limitations of claims 21-25 herein where the protease of SEQ ID NO:2 of Lassen et al. **'630** constitutes a variant of SEQ ID NO:2 herein that may share as much as 60% amino acid sequence identity with SEQ ID NO:2 herein.

e. Claims 1, 2, 4, 11, 15, 16, 28-31 and 37 herein are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of **US 7,208,310**, made of record herewith. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 2, 4, 11, 15, and 16 pending herein are drawn to a protease variant having at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2 herein, an animal feed additive comprising such a variant and at least one among three further components, an animal feed composition comprising such a feed additive and a crude protein content in a range of 50 to 800 g/kg, a method for improving the nutritional value of an animal feed by adding such a protease variant to the feed, a method for treating proteins comprising adding the protease variant to the proteins, and a detergent composition comprising such a protease variant and because the patented claims 1 and 9 are drawn to an isolated protease, or variant thereof, having an amino acid sequence that is at least 95% identical to the sequence of positions 1-188 of SEQ ID NO:2 of the patent, a protease that meets the limitations of claims 1, 2, 4, 11, 15, and 16 herein where it is the same *Nocardiopsis alba* DSM 15647 protease of SEQ ID NO:12 of Lassen et al. **'630**, discussed above, while the patented claim 4 is

drawn to an animal feed additive comprising such a protease or variant and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral according to claim 28 herein which, when added to an animal feed composition of the patented claim 6 will improve the nutritional value of such an animal feed according to claim 30 herein and will inherently constitute a method of treating proteins according to claim 31 herein where, according to the patented claims 5 and 6, may have a crude protein content of 50 to 800 g/kg, meeting limitations of claim 29 herein, and because the patented claim 8 is drawn to a detergent composition comprising a surfactant and protease of the patented claim 1 that meets limitations of claims 1, 2, 4, 11, 15, and 16 herein, thus is a detergent composition according to claim 37 herein.

f. Claims 21-25 herein are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over at least claim 1 of **US 7,208,310**, in view of Wilson et al., **US 5,705,379**, discussed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims 21-25 are drawn a nucleic acid sequence that encodes a protease variant having at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2, an expression construct comprising such a coding sequence and control regions, an expression vector comprising such a construct, a recombinant host cell that comprises such a vector, a method of making the encoded variant comprising cultivating such a host cell and recovering the protease variant and because at the patented claim 1 is drawn to an isolated protease, or variant thereof, having an amino acid sequence that is at least 95% identical to the sequence of positions 1-188 of SEQ ID NO:2 of the patent, a protease that meets the limitations of claims 1, 2, 4, 11, 15, and 16 herein. The teachings of Wilson et al. are taken as before. It would have been obvious to one of ordinary skill in the art to prepare a nucleic acid construct linking a DNA sequence encoding the protease of Lassen et al. **'310** to (a) control sequence(s) that can direct the expression of the protease-encoding DNA region in a host cell, place the construct in an expression vector, transform a suitable host cell with the expression vector, cultivate the host cell to permit production of the encoded protease whereby the mature protease is produced in the supernatant, and to then recover and isolate the protease so that it may be used in industrial processes, according to the teachings of Wilson et al., meeting limitations of claims 21-25 herein where the protease of SEQ ID NO:2 of Lassen et al. **'310** constitutes a variant of SEQ ID NO:2 herein that may share as much as 60% amino acid sequence identity with SEQ ID NO:2 herein

g. Claims 1, 2, 4, 11, 15, 16, 21-25, and 28-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 10-17, and 19 of Lassen, **US 7,485,447**, discussed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims are drawn to a protease variant **comprising** an amino acid sequence that shares at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2 herein, a nucleic acid sequence encoding such a variant, an expression construct comprising such a coding sequence, an expression vector that comprises such a construct, a recombinant host cell comprising such a vector, a method of making the encoded variant comprising cultivating such a host cell and recovering the protease variant an animal feed additive comprising such a variant and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral, an animal feed composition comprising such a feed additive and a crude protein content in a range of 50 to 800 g/kg, a method for improving the nutritional value of an animal feed by adding such a protease variant to the feed, a method for treating proteins comprising adding the protease variant to the proteins, and because the patented claims 1-7, 10-17, and 19 are drawn to an isolated protease, or variant thereof, **comprising** an amino acid sequence that is at least 95% identical to the sequence of positions 1-188 of either of SEQ IDs NOs:37 or 41 of the patent, proteases that meet the limitations of claims 1, 2, 4, 11, 15, and 16 herein where they are the same proteases of SEQ IDs NOs:37 and 41 of Lassen **'447**, discussed above, and drawn as well to nucleic acid sequences encoding such proteases, expression constructs comprising such coding sequences, expression vectors comprising such constructs, recombinant host cells comprising such vectors, methods of making the encoded proteases comprising cultivating such host cells and recovering the proteases, according to claims 21-25 herein, animal feed additives comprising such proteases and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral according to claim 28 herein, which, when added to an animal feed composition of the patented claim 6 will improve the nutritional value of such an animal feed according to claim 30 herein and will inherently constitute a method of treating proteins according to claim 31 herein where, according to the patented claims 5 and 6, may have a crude protein content of 50 to 800 g/kg, meeting limitations of claim 29 herein.

h. Claim 37 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over at least claim 1 of **US 7,485,447**, in view of Anderson et al., **EP 0 506 448**, discussed above. Although the conflicting claims are not identical, they are not patentably

distinct from each other because the pending claim 37 is drawn to a detergent composition that comprises a surfactant and a protease variant having at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2 and because the patented claim 1 is drawn to an isolated protease, or variant thereof, **comprising** an amino acid sequence at least 95% identical to the sequence of positions 1-188 of either of SEQ IDs NOs:37 or 41 of the patent, proteases meeting limitations of claims 1, 2, 4, 11, 15, and 16 herein where they are the same proteases of SEQ IDs NOs:37 and 41 of Lassen **'447**, discussed above. The teaching of Anderson et al., discussed above, is taken as before. It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a detergent composition that comprises a protease of Lassen **'447** and a surfactant because Anderson et al. teach that thermostable, alkaline pH-stable, microbial proteases, and their variants, known to be useful in industrial processes are advantageously combined with surfactants in detergent compositions.

i. Claims 1, 2, 4, 11, 15, 16, 21-25, 28-31, and 37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 8-11, and 14-24 of Oestergaard et al., **US 7,588,926**, made of record herewith. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims 1, 2, 4, 11, 15, 16, 21-25, 28-31, and 37 are drawn to a protease variant that shares at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2, a nucleic acid sequence encoding such a variant, an expression construct comprising such a coding sequence, an expression vector comprising such a construct, a recombinant host cell comprising such a vector, a method of making the encoded variant comprising cultivating such a host cell and recovering the protease variant, an animal feed additive comprising such a variant and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral, an animal feed composition comprising such a feed additive and a crude protein content in the range of 50 to 800 g/kg, a method for improving the nutritional value of an animal feed by adding such a protease variant to the feed, a method for treating proteins comprising adding a protease variant to the proteins, and a detergent composition comprising such a protease variant and because the patented claims 1-5 and 8-11 are drawn to a protease with an amino acid sequence at least 97% identical to SEQ ID NO:6 of the patent or a protease with an amino acid sequence at least 97% identical SEQ ID NO:8 of the patent which are also proteases of claims 1, 2, 4, 11, 15, and 16 herein

where SEQ ID NO:2 herein shares 98.6% identity and 99.4% identity with, respectively, SEQ IDs NOs:6 and 8 of the patent, and also because the patented claims 14-24 are drawn to nucleic acid sequences encoding either protease of the patented claim 1, expression constructs comprising such coding sequences and expression vectors comprising such constructs, as well as recombinant host cells comprising such vectors and methods of making either encoded protease comprising cultivating such host cells and recovering a protease, animal feed additives comprising such proteases and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral, an animal feed composition comprising such a feed additive and a crude protein content in the range of 50 to 800 g/kg, where a method for improving the nutritional value of an animal feed by adding such a protease variant to the feed is inherently incorporated by incorporating either protease in the composition, which is also inherently a method for treating proteins comprising adding either protease to proteins of the animal feed composition, and a detergent composition comprising such a protease variant.

The following rejections are <u>provisional</u> obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

j. Claims 1, 2, 4, 11, 15, 16, 21-25, and 28-31 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 11, 12, and 14-19 of the copending Application No. 11/570,193, made of record herewith as its Pre-Grant Publication **US 2008/0286415**. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 2, 4, 11, 15, 16, 21-25, and 28-31 pending herein are drawn to a protease variant that shares at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2, a nucleic acid sequence encoding such a variant, an expression construct comprising such a coding sequence, an expression vector comprising such a construct, a recombinant host cell comprising such a vector, a method of making the encoded variant comprising cultivating such a host cell and recovering the protease variant, an animal feed additive comprising such a variant and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral, an animal feed composition comprising such a feed additive and a crude protein content in the range of 50 to 800 g/kg, a method for improving the nutritional value of an animal feed by adding such a protease variant to the feed, a method for treating proteins comprising adding a protease variant to the proteins, and a detergent composition comprising such a protease variant and because the claims 1-3 of the copending application are drawn to any of four proteases – of SEQ IDs NOs:2, 4, 6 and 8 – each of which must have an

amino acid sequence at least 71.5% identical to SEQ ID NO:6 of the copending application, which amino acid sequence is the most distant from that of SEQ ID NO:2 herein which shares 67.3% identity with the copending SEQ ID NO:6, thus the amino acid sequences of the copending claims 1-3 constitute protease variants of claims 1, 2, 4, 11, 15, 16 herein, and also because the copending claims 4-8, 11, 12, and 14-19 are drawn to a nucleic acid sequence encoding a protease of copending claim 1, an expression construct comprising such a coding sequence and an expression vector comprising such a construct, a recombinant host cell comprising such a vector and a method of making an encoded protease comprising cultivating such a host cell and recovering a protease, animal feed additives comprising such proteases and at least one of a fat soluble vitamin, a water soluble vitamin, or a trace mineral, an animal feed composition comprising such a feed additive and a crude protein content in the range of 50 to 800 g/kg, a method for improving the nutritional value of an animal feed by adding such a protease variant to the feed and a method for treating proteins comprising adding either protease to proteins of the animal feed composition.

k. Claim 37 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over at least claim 1 of the copending Application No. 11/570,193, in view of Anderson et al., **EP 0 506 448**, both discussed above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claim 37 is drawn to a detergent composition that comprises a surfactant and a protease variant having at least 60% identity with SEQ ID NO:2 herein and differing from the amino acid sequence of SEQ ID NO:2 at one or more of 44 amino acid positions within any array corresponding to amino acid positions **78-100**, **103-106**, **111-114**, and **118-131** of SEQ ID NO:2 and because the copending claim 1 is drawn to an isolated protease having an amino acid sequence at least 71.5% identical to the sequence of the copending application's SEQ ID NO:6, which protease meets limitations of claims 1, 2, 4, 11, 15, and 16 herein where a protease of SEQ ID NO:2 herein shares 67% identity with the amino acid sequence of copending SEQ ID NO:6. The teaching of Anderson et al., discussed above, is taken as before. It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a detergent composition that comprises a protease of the copending application and a surfactant because Anderson et al. teach that thermostable, alkaline pH-stable, microbial proteases, and their variants, known to be useful in industrial processes are advantageously combined with surfactants in detergent compositions.

Conclusion

Claim 5 is objected to as being dependent upon a rejected base claim, where its elected and examined subject matter, i.e., the paired substitutions 76C+85C, 94C+149C, 6C+103C, 8C+105C, and 106C+141C, is free of the prior art of record herein, thus the claim would be allowable if rewritten in independent form directed to the elected subject matter and including all of the limitations of the base claim and any intervening claims.

While Lassen et al. **US 7,208,310**, and Oestergaard et al. **US 7,588,926**, are both made of record herewith, citation of the **'310** and **'926** patents in separate prior art rejections would be redundant because they share a common disclosure in the 29 June 2003-filed US provisional application 60/480,096 of the same *Nocardiopsis dassonvillei* DSM 43235 protease of SEQ ID NO:2 of Lassen et al. **'630**, discussed above, i.e., in SEQ ID NO:6 of Lassen et al. **'310** and in SEQ ID NO:12 of Oestergaard et al. **'926**.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Andrew Wang, can be reached at 571.272.0811. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

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